2407404

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DNA sequence encod
DNA encoding human
Codon-optimised RA
Human alpha-1-tryp
                                                                                                                                              December 6, 2002, 16:39:25 ; Search time 231.5 Seconds (without alignments) 14834.978 Million cell updates/sec
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                                                                                                                                                                                                                                                                                                                  1 tctagaccatggaagaccct.......ccagtcaaggcctagtcgac 1525
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GenCore version 5.1.3 Copyright (c) 1993 - 2002 Compugen Ltd.
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            This invention relates to a novel fusion protein comprising a first protease inhibitor comprising an alphal-antitrypsin or its functionally active portion and a second protease inhibitor or its functionally active protein. The fusion proteins of the invention may act as an inhibitor of protease activity. The fusion protein of the invention is useful for inhibiting protease activity associated with a disorder such as emphysem, asthma, chronic obstructive pulmonary disease, cystic fibrosis, otitis media, otitis external or HIV infection, or for intenting an individual suffering from or at risk for a disease or disorder involving unwanted protease activity. The proteins are useful for treating dermatological diseases such as atopic dermatitis, eczema
                                                                                                                                                                                                                                                                                                                                                                                                                       Novel fusion protein useful for inhibiting protease activity associated with a disorder such as emphysema, asthma, comprises a first protease inhibitor comprising alpha 1-antitrypsin and a second protease inhibitor -
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20-NOV-2001; 2001US-331966P.
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Matches 1525; Conservative
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                                                                                 GTTTATTTTTGTCTGAAGGTTTAAAATTGGTTGACAAATTCCTAGAAGACGTCAAGAAAC
                                                                                                                                       TATATCATAGTGAGGCTTTTACCGTTAATTTTGGTGATACTGAGGAAGCTAAAAAGCAAA
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                           301 AAGAGTTGTTGAGAACTTTGAATCAACCTGATTCTCAATTGCAATTAACTACTGGTAACG
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rN-TAP1; gene; ds; Alzheimer's disease; tumour anglogenesis; malaria; emphysema; asthma; chronic obstructive pulmonary disease; cystic fibrosis; otitis media; otitis external; HIV; psoriasis; eczema; human immunodeficiency virus; atopic dermatitis; muscular dystrophy; herpes; ulceration; sepsis; rhummatoid arthritis; periodontal disease; tumour metastasis; osteoporosis; Paget's disease; scleroderma; glomerulonephritis; hypertension.
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                               GTAAGTGTCCAGTTACTTACGGTCAATGTTTGATGTTGAACCCACCAAACTTCTGTGAAA
                                                                                                               TGGACGGTCAATGTAAGAGAGTCTTGAAGTGTTGTATGGGTATGTGTGGTAAGTCCTGTG
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9.1577
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/note= "TIMP-1 coding region"
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This invention relates to a novel fusion protein comprising a first protease inhibitor comprising an alphal-antitrypsin or its functionally active portion and a second protease inhibitor or its functionally active protein. The fusion proteins of the invention may act as an inhibitor of protease activity. The fusion protein of the invention is useful for inhibiting protease activity associated with a disorder. So such as emphysema, asthma, chronic obstructive pulmonary disease, costic fibrosis, otilis media, otilis external or HIV infection, or for treating an individual suffering from or at risk for a disease or disorder involving unwanted protease activity. The proteins are useful for treating dermatological diseases such as atopic dermatitia, eczam and psoriasis, in infilammatory responses to viral infection, and for treating herpes infection, corneal or epidermal ulceration, chronic con-healing wounds, sepsis, rhemmatoid arthritis, periodontal disease, turnour metastasis and tumour anglogenesis, apstric ulceration, and disease.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         osteoporosis, Paget's disease, glomerulonephritis, scleroderma, malaria, bacterial infection, Alzhaimer's disease, hypertension and muscular dystrophy. The present sequence represents the DNA encoding the IN-TAPI fusion protein of the invention.
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                                                                                                                                                AGAACGAGGATCGTCGTAGCGCTTCTCTGCACCTGCCAAAGTTAAGTATCACCGGTACTT
                                                                                                                                                                      ACGACITAAAAAICIGITITAAGGCCAGITAAGGTATTACCAAAGTITTITCTAACGGTGCCG
                                   /standard_name= "Ribosome binding 9..1751
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            product "rTAP1 fusion protein" 2..1193
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/note= "TIMP-1 coding region"
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               DNA sequence encoding rTAP1 fusion protein.
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/note= "AAT coding region"
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'note= "linking codon"
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This invention relates to a novel fusion protein comprising a first protease inhibitor comprising an alphal-antitrypsin or its functionally active portion and a second protease inhibitor or its functionally active protein. The fusion proteins of the invention may act as an inhibitor of protease activity. The fusion protein of the invention is useful for inhibiting protease activity associated with a disorder such as emphysema, asthma, chronic obstructive pulmonary disease, cystic fibrosis, ottis media, oftis external or HIV infection, or for treating an individual suffering from or at risk for a disease or disorder involving unwanted protease activity. The proteins are useful for treating dermatological diseases such as atopic dermatitis, eczema and psoriasis, in inflammatory responses to viral infection, and for treating herees infection, corneal or epidermal ulceration, chronic con-healing wounds, sepsis, rhemmatoid arthritis, periodontal disease, themselves and tumour metastasis and tumour anglogenesis, quartic ulceration,
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           osteoporosis, Paget's disease, glomerulonephritis, scieroderma, malaria, bacterial infection, Alzheimer's disease, hypertension and muscular dystrophy. The present sequence represents the DNA encoding the
                                                                                                                                                                                                                                                                                     Novel fusion protein useful for inhibiting protease activity associated with a disorder such as emphysema, asthma, comprises a first protease inhibitor comprising alpha 1-antitrypsin and a second protease inhibitor -
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            181 TIGCCACTGCTTTCGCCATGTTGAGTTTAGGTACTAAAGCCGATACCCATGACGAGATTT
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0; Mismatches
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                                                                                                                  18-DEC-2000; 2000US-256699P.
20-NOV-2001; 2001US-331966P.
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Matches 1198; Conservative
                                                                                                                                                                      (ARRI-) ARRIVA PHARM INC.
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        AAGTICCAAIGAAAAAGACIGGGIAIGIICAAIAIICAACAIIGCAAAAAIIAAGII 720
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                                 TATATCATAGTGAGGCTTTTACCGTTAATTTTGGTGATACTGAGGAAGCTAAAAGCAAA
                                                                                                  ATCGTGATACCGTCTTCGCACTAGTTAACTATATTTTTTCAAGGGTAAGTGGGAACGTC
                                                                                                                                   CTTTCGAGGTTAAAGATACTGAAGAAGAATTTTCATGTTGATCAAGTTACTACTGTCA
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This invention relates to a novel fusion protein comprising a first protease inhibitor comprising an alphal-antitrypsin or its functionally active portion and a second protease inhibitor or its functionally active protein. The fusion proteins of the invention may act as an inhibitor of protease activity. The fusion protein of the invention as an active protein of protease activity associated with a disorder such as emphysema, asthma, chronic obstructive pulmonary disease.

Such as emphysema, asthma, chronic obstructive pulmonary disease.

Cystic fibrosis, otitis media, otitis external or HIV infection, or for treating an individual suffering from or at risk for a disease or disorder involving unwanted protease activity. The proteins are useful for treating dermatological diseases such as atopic dermatitis, eczema and psoriasis, in inflammatory responses to viral infection, and for treating herpes infection, corneal or epidermal ulceration, chronic non-healing wounds, sepsis, rheumatoid arthritis, periodomial disease, tumour metastasis and tumour anglogenesis, gastic ulceration, the corneal or epidermal infection, more consis, paget's disease, hypertension and muscular anglogenesis, the construction and muscular and and processed and tumour anglogenesis, the protection and muscular and and processed and processe
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     Novel fusion protein useful for inhibiting protease activity associated with a disorder such as emphysema, asthma, comprises a first protease inhibitor comprising alpha 1-antitrypsin and a second protease
tumour metastasis; tumour angiogenesis; osteoporosis; Paget's disease; glomerulonephritis; scleroderma; hypertension.
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99.7%; Pred. No. 1.6e-289;
tive 0; Mismatches 4;
                                                                                                                                                                                                                                                                                          'product- "SLAP1 fusion protein"
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note= "SLPI coding region"
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/note= "AAT coding region"
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/note- "linking codon"
336..1517
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                                                                                                                                              Location/Qualifiers
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P-PSDB; AAU99881.
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                                                                       Homo sapiens.
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malaria; emphysema; asthma; chronic obstructive pulmonary disease; cystic fibrosis; otitis media; otitis external; HIV; psoriasis; eczema; human immunodeficiency virus; atopic dermatitis; muscular dystrophy; herpes; ulceration; sepsis; rheumatoid arthritis; periodontal disease;

ö 4; Indels Matches 1194; Conservative

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1405 CAATGAGCATTCCACCAGAAGTTAAATTTAATAAACCATTCGTTTTTCTGATGATCGAGC 1464

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CAATGAGCATTCCACCAGAAGTTAAATTTAATAAACCATTCGTTTTTTCTGATGATCGAGC 1140
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                                                                                            TAGAAGGITTAAACTTTAATTTGACCGAAATCCCAGAAGCCCAAATTCACGAGGGTTTTC
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Novel fusion protein useful for inhibiting protease activity associated with a disorder such as emphysema, asthma, comprises a first protease inhibitor comprising alpha 1-antitrypsin and a second protease
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                protease inhibitor comprising an alphal-antitrypsin or its functionally active portion and a second protease inhibitor or its functionally active protein. The fusion proteins of the invention may act as an inhibitor of protease activity. The fusion protein of the invention
                                                                                                                                                                                       TAPI; gene; ds; Alzheimer's disease; tumour angiogenesis; malaria; emphysema; asthma; chronic obstructive pulmonary disease; cystic fibrosis; otitis media; otitis external; HIV; psoriaais; eczema; human immunodeficiency virus; atopic dermatitis; muscular dystrophy; herps; ulceration; sepsis; rheumatoid arthritis; periodontal disease; tumour metaatasis; osteoporosis; Paget's disease; scleroderma; glomerulonephritis; hypertension.
This invention relates to a novel fusion protein comprising a first
                                                                                                                                                                                                                                                                                                                                                                        "Ribosome binding site"
                                                                                                                                                                                                                                                                                                                                                                                                              'product- "TAP1 fusion protein"
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/note= "TIMP-1 coding region"
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/note= "AAT coding region"
                                                                                                                                                                     protein.
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/note= "linking codon"
567..1748
                                                                                                                                                                                                                                                                                                                                   Location/Qualifiers
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                                                                                                                                                                       DNA sequence encoding TAP1 fusion
                                                                                                                                                                                                                                                                                                                                                                        /standard_name=
9..1751
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                                                                                            ABK88023 standard; DNA; 1756
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2001US-331966P
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         18-DEC-2001; 2001WO-US49256
                                                                                                                                               (first entry)
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          WPI; 2002-500631/53
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                                                                                                                                                                                                                                                                                                  Homo sapiens.
Synthetic.
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     inhibitor
                                                                                                                      ABK88023;
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                                                                                  ABK8802
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such as emphysems, asthma, forconic obstructive pulmonary disease, ystic fibrosis, otitis media, otitis external or HIV infection, or for treating an individual suffering from or at risk for a disease or disorder involving unwanted protease activity. The proteins are useful for treating dermatological diseases such as atopic dermatitis, eczema and psoriasis, in inflammatory responses to viral infection, and for treating herpes infection, corneal or epidermal ulceration, chronic non-healing wounds, sepsis, rheumatoid arthritis, periodontal disease, osteoporosis, paget's disease, glomerulonophritis, scleroderma, malaria, bacterial infection, Alzheimer's disease, hypertension and muscular dystrophy. The present sequence represents the DNA encoding the TAPI fusion protein of the invention.
useful for inhibiting protease activity associated with a disorder
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Sequence 1756 BP; 493 A; 395 C; 373 G; 495 T; 0 other;

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                                                   ACCATCCGACTTTTAATAAAATTACTCCAAATTTAGCCGAATTTGCTTTTTCTTTGTATA 126
                                                                                           CTGCTTTCGCCATGTTGAGTTTAGGTACTAAAGCCGATACCCATGACGAGATTTTAGAAG 246
                                                                                                                                                                                                                                861
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                       Gaps
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                                                                                                                                                                                                        GTTTAAACTTTAATTTGACCGAAATCCCAGAAGCCCAAATTCACGAGGGTTTTCAAGAGT
                                                                                                                                                                                                                                                                                                    ATACCGTCTTCGCACTAGTTAACTATATTTTTCAAGGGTAAGTGGGGACGTCCTTTCG
                                                                                                                                                                                                                                                                                                                                                                                                                                   1102 ATACCGTCTTCGCACTAGTTAACTATTTTTTCAAGGGTAAGTGGGAACGTCCTTTCG
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        GTTTAAACTTTAATTTGACCGAAATCCCAGAAGCCCAAATTCACGAGGGTTTTCAAGAGT
                                                                                                                                                                                                                                                 TGTTGAGAACTTTGAATCAACCTGATTCTCAATTGCAATTAACTACTGGTAACGGTTTAT
                                                                                                                                                                                                                                                                                         TITIGICIGAAGGITIAAAATIGGITGACAAATICCIAGAAGACGICAAGAACTATAIC
                                                                                                                                                                                                                                                                                                                                 ATAGTGAGGCTTTTACCGTTAATTTTGGTGATACTGAGGAAGCTAAAAAGCAAATTAATG
                                                                                                                                                                                                                                                                                                                                                                         ATTATGTTGAGAAAGGCACCCAGGGTAAGATCGTTGACCTAGTTAAAGAATTAGATCGTG
                                                                                                                                                                                                                                                                                                                                                                                                                                                         AGGTTAAAGATACTGAAGAGGAAGATTTTCATGTTGATCAAGTTACTACTGTCAAAGTTC
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 CAATGATGAAAAGACTGGGTATGTTCAATATTCAACATTGCAAAAATTAAGTTCTTGGG
78.0%; Score 1188.8; DB 24; Length 1756; 99.8%; Pred. No. 8.3e-289; tive 0; Mismatches 2; Indels 0;
                                                                                                                                                                                                                    Best Local Similarity 99.8 Matches 1190; Conservative
  Query Match
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NTAP1; gene; ds; Alzheimer's disease; tumour angiogenesis; malaria; emphysema; asthma; chronic obstructive pulmonary disease; cystic fibrosis; otitis media; otitis external; HIV; psoriasis; eczema; human immunodeficiency virus; atopic dermathiis; muscular dystrophy; herpes; ulceration; sepsis; rheumatoid arthritis; periodontal disease; tumour metastasis; osteoporosis; Paget's disease; scleroderma;
                                                                                                                                                                                       GTGGTGTTACTGAAGAAGCTCCATTAAAATTGAGTAAAGCTGTTCACAAAGCCGTCTTAA 1026
                                                                                                                                           CTATTGATGAAAAGGGTACCGAGGCCGCCGGCGCTATGTTCCTGGAAGCTATTCCAATGA 1086
                                                                                                                                                                                                                     GCATTCCACCAGAAGTTAAATTAATAAACCATTCGTTTTTCTGATGATCGAGCAGAACA 1146
                                                                                                                                                                                                                                1642 GCATTCCACCAGAAGTTAAAATTAAAACCATTCGTTTTTTCTGATGATCGAGCAGAACA 1701
                                                                                      AGCTTCAACATTTAGAGAATGAGTTGACTCATGACATTATTACTAAATTTTTAGAGAACG
                                           AGGATCGTCGTAGCGCTTCTCTGCACCTGCCAAAGTTAAGTATCACCGGTACTTACGACT
                                                                                                                                                                                                                                                              site"
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/standard_name= "Ribosome binding
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    "NTAP1 fusion protein
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           /*tag= c
/note= "TIMP-1 coding region"
                                                                                                                                                                                                                                                                                                                                                                                                           DNA sequence encoding N-TAP1 fusion protein.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     'note= "AAT coding region"
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/note= "linking codon"
393..1574
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       Location/Qualifiers
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 glomerulonephritis; hypertension.
                                                                                                                                                                                                                                                                                                                                            BP
                                                                                                                                                                                                                                                                                                                                           ABK88024 standard; DNA; 1582
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/product= "
12..389
                                                                                                                                                                                                                                                                                                                                                                                     07-OCT-2002 (first entry)
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18-DEC-2001; 2001WO-US49256

us-10-025-514-15\_1.rng

805 ATCATAGTGAGGCTTTTACCGTTAATTTTGGTGATACTGAGGAAGCTAAAAAGCAAATTA

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This invention relates to a novel fusion protein comprising a first protease inhibitor comprising an alphal-antitrypain or its functionally active portion and a second protease inhibitor or its functionally active protein. The fusion proteins of the invention may act as an inhibitor of protease activity. The fusion protein of the invention is useful for inhibiting protease activity associated with a disorder such as emphysema, asthma, chronic obstructive pulmonary disease, cystic fibrosis, otitis media otitis external or HIV infection, or for treating an individual suffering from or at risk for a disease or city treating dermatological diseases such as atopic dermatitis, eczema and psoriasis, in inflammatory responses to viral infection, and for treating herpes infection, corneal or epidermal ulceration, chronic treating wounds, sepsis, rhemmatoid arthritis, periodontal disease, tumour metastasis and tumour angiogenesis, gastric ulceration, malasia
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        osteoporosis, Paget's disease, glomerulonephritis, scleroderma, malaria, bacterial infection, Alzheimer's disease, hypertension and muscular dystrophy. The present sequence represents the DNA encoding the NTAPI fusion protein of the invention.
                                                                                                                                                                            Novel fusion protein useful for inhibiting protease activity associated with a disorder such as emphysema, asthma, comprises a first protease inhibitor comprising alpha 1-antitrypsin and a second protease
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            243
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   AGTIGITGAGAACTITGAATCAACCTGATTCTCAATTGCAATTAACTACTGGTAACGGTT 363
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            AAGACCATCCGACTTTTAATAAATTACTCCAAATTTAGCCGAATTTGCTTTTTCTTTGT 123
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  63
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           364 TATTTTTGTCTGAAGGTTTAAAATTGGTTGACAAATTCCTAGAAGACGTCAAGAAACTAT
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       Sequence 1582 BP; 464 A; 333 C; 329 G; 456 T; 0 other;
                                                                                                                                                                                                                                                                        Example 2; Page 85-86; 134pp; English.
                                                                                       Pemberton P;
18-DEC-2000; 2000US-256699P.
20-NOV-2001; 2001US-331966P.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                Matches 1190; Conservative
                                                   (ARRI-) ARRIVA PHARM INC
                                                                                         Gibson HL,
                                                                                                                           2002-500631/53
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                Local Similarity
                                                                                                                                                P-PSDB; AAU99883
                                                                                                                                                                                                                                       inhibitor
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                                                                                           Barr PJ,
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Alpha-1-antitrypsin; AAT; human; gene; ds; protease inhibitor; malaria; emphysema; asthma; chronic obstructive pulmonary disease; eczema; cystic fibrosis; otitis media; otitis external; HIV; psoriasis; human immunodeficiency virus; atopic dermatitis; muscular dystrophy; herpes; ulceration; sepsis; rheumatoid arthritis; periodontal disease; tumour metastasis; tumour angiogenesis; osteoporosis; Paget's disease; glomerulonephritis; scleroderma; Alzheimer's disease; hypertension.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                               1464
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       1084 IGAGCATTCCACCAGAAGTTAAATTTAATAAACCATTCGTTTTTCTGATGATCGAGCAGA 1143
                                                                                                                                                                                                                                                                                                                                                                                                                                                      1024 TAACTATTGAAGAAAGGGTACCGAGGCCGCGCGCGCTATGTTCCTGGAAGCTATTCCAA 1083
                                                                                                                                                                                                                                                                                                                                                               GTAAGCITCAACATTTAGAGAATGAGITGACTCATGACATTATTACTAAATTTTTAGAGA 843
                                                                                                                                                                                                                                                                                                                                                                                                     TGAGTGGTGTTACTGAAGAAGCTCCATTAAAATTGAGTAAAGCTGTTCACAAAGCCGTCT
                                                                                                                                                                                                                                                                                                                                                                                                                                                                     1465 TGAGCATTCCACCAGAAGTTAAATTTAATAAACCATTGGTTTTTCTGATGAGCAGAGA
           GTGATACCGTCTTCGCACTAGTTAACTATATTTTTTCAAGGGTAAGTGGGAACGTCCTT
                                                            TCGAGGTTAAAGATACTGAAGAGGAAGATTTTCATGTTGATCAAGTTACTACTGTCAAAG
                                                                                                                                                                                                    844 ACGAGGATCGTCGTAGCGCTTCTCTGCACTGCCAAAGTTAAGTATCACCGGTACTTACG
                                                                                                                                                                                                                                                                                                                                                     ACTITAAAATCTGTTTTAGGCCAGTTAGGTATTACCAAAGTTTTTTCTAACGGTGCCGATT
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           1144 ACACTAAAAGCCCATTGTTTATGGGTAAGGTTGTCAACCCCAACTCAGAAGATGTC 1198
ATGATTATGTTGAGAAAGGCACCCAGGGTAAGATCGTTGACCTAGTTAAAGAATTAGATC
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         DNA encoding human alpha-1-antitrypsin (AAT) protein.
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ATCATAGTGAGGCTTTTACCGTTAATTTTGGTGATACTGAGGAAGCTAAAAAGCAAATTA 483

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/note= "No start or stop codon shown" /product= "Alpha-1-antitrypsin" /partial

WO200250287-A2

27-JUN-2002

18-DEC-2001; 2001WO-US49256

18-DEC-2000; 2000US-256699P. 20-NOV-2001; 2001US-331966P.

(ARRI-) ARRIVA PHARM INC

Pemberton P; Gibson HL, Barr PJ,

WPI; 2002-500631/53 P-PSDB; AAU99873. Novel fusion protein useful for inhibiting protease activity associated with a disorder such as emphysema, asthma, comprises a first protease inhibitor comprising alpha 1-antitrypsin and a second protease Inhibitor

Disclosure; Page 24-25; 134pp; English.

This invention relates to a novel fusion protein comprising a first protease inhibitor comprising an alphal-antitrypsin or its functionally active portion and a second protease inhibitor or its functionally active protein. The fusion protease inhibitor or its functionally is useful for inhibitor protease activity. The fusion protein of the invention may act as an is useful for inhibiting protease activity associated with a disorder of contracting an individual suffering from or at risk for a disease or for treating an individual suffering from or at risk for a disease or contracting dermatological diseases activity. The proteins are useful for treating dermatological diseases such as atopic dermatitis, eccam and psoriasis, in inflammantory responses to viral infection, and for treating herpes infection, corneal or epidermal ulceration, chronic con-healing wounds, sepsis, rheumatoid arthritis, periodontal disease, tunnur metastasis and tunour anglogenesis, gastric ulceration, maistic contraction categories. osteoporosis, Paget's disease, glomerulonephritis, scleroderma, malaria, bacterial infection, Alzheimer's disease, hypertension and muscular dystrophy. The present sequence represents the DNA encoding the human alpha-1-antitrypsin (AAT) protein used to create the fusion protein of the invention. 

Sequence 1182 BP; 369 A; 214 C; 229 G; 370 T; 0 other;

ö 121 Tragcreargraarreracracracarrittragreergriteratigeeacrgci 180 TTCGCCATGTTGAGTTTAGGTACTAAAGCCGATACCCATGACGAGATTTTAGAAGGTTTA 251 AACTTTAATTTGACCGAAATCCCAGAAGCCCAAATTCACGAGGGTTTTCAAGAGTTGTTG 311 132 TTAGCTCATCAAAGTAATTCTACTAACATTTTTTTAGTCCTGTTTCTATTGCCACTGCT 191 Gaps 12 GAAGACCCTCAAGGCGACGCCGCTCAAAAACCGACACCAGTCATCACGACCAAGACCAT ö Length 1182; Indels 77.5%; Score 1182; DB 24; 100.0%; Pred. No. 3.7e-287; tive 0; Mismatches 0; Matches 1182; Conservative Best Local Similarity Query Match 192 252 g ò 8 ò g ð ð 용 ò

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GATGAAAAGGGTACCGAGGCCGCCGGCGCTATGTTCCTGGAAGCTATTCCAATGAGCATT 1091
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                                                                                                                                                                                                                                                                                                                                                                                                                                                              GTIACTGAAGAAGCTCCATTAAAATTGAGTAAAGCTGTTCACAAAGCCGTCTTAACTATT 1031
                              AAAGATACTGAAGAGGAAGATTTTCATGTTGATCAAGTTACTGTGTGAGTTCCAATG 671
                                                                                                                                                                                                                                                                                                                                                                                960
241 AACTTTAATTTGACCGAAATCCCAGAAGCCCAAATTCACGAGGGTTTTCAAGAGTTGTTG 300
                                                                     ATGAAAAGACTGGGTATGTTCAATATTCAACATTGCAAAAAATTAAGTTCTTGGGTCTTA 731
                                                                                                                                                                                                                                                                                661 ATGAAAAGACTGGGTATGTTCAATATTCAACATTGCAAAAAATTAAGTTCTTGGGTCTTA 720
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                   AGAACTTTGAATCAACCTGATTCTCAATTGCAATTAACTACTGGTAACGGTTTATTTTG 371
                                                           TCTGAAGGTTTAAAATTGGTTGACAAATTCCTAGAAGACGTCAAGAAACTATATCATAGT 431
                                                                                                  GAGGCTTTTACCGTTAATTTTGGTGATACTGAGGAAGCTAAAAAGCAAATTAATGATTAT 491
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                                                                                                                                                    TCTGTTTTAGGCCAGTTAGGTATTACCAAAGTTTTTTTTAAAGGGGCCGATTTAGAGTGTT
                                                                                                                                          GTTGAGAAAGGCACCCAGGGTAAGATCGTTGACCTAGTTAAAGAATTAGATCGTGATACC
                                                                                                                                                                                                                                                                                                                                           CAACATTTAGAGAATGAGTTGACTCATGACATTATTACTAAATTTTTAGAGAACGAGGAT
                                                                                                                                                                                                                                                                                                                                                                                                                                         Codon-optimised RAmy3D signal fused to DNA encoding mature AAT.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             1152 AGCCCATTGTTTATGGGTAAGGTTGTCAACCCAACTCAGAAG 1193
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Mon Dec

196 CTCGCGCACCAGTCCAACTCCACCAACATCTTCAGCCCGGTGAGCATCGCCACCGCC 255

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to exemplify the invention. The specification describes a method for producing mature alphal-antitypsin (AAT). The protein is used to producing mature heterologues protein in monocotyledonous plant cells. The method comprises transforming the cells with a chimeric gene comprising a monocotyledon transcription regulator, inducible either during seed maturation or by adding/removing a small molecule, DNA encoding the heterologues protein, and DNA encoding a signal peptide, with the signal peptide causing secretion of the protein from the cell. The proteins expressed in this manner include mature glycosylated alpha proteins expressed in this manner include mature glycosylated alpha increases its serum half-life, mature glycosylated antithrombin III (ATII), mature human serum albumin (HSA) having the native folding pattern as shown by bilirubin-binding characteristics, or mature active subtilisin BPN'. These proteins are useful therapeutically (e.g. AAT for treating emphysema, ATIII as antithrombotic and HSA as blood replacement) or as industrial enzymes (BPN' is used in detergents).
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               The present sequence encodes a fusion protein of codon-optimised RAmy3D
Protein expression; monocotyledon plant cell; glycosylated alpha 1-antitrypsin; AT; glycosylated alpha 1-antitrypsin; AT; glycosylated artithrombin III; ATIII; human serum albumin; HSA; subtilisin BBN'; treatment; emphysema; antithrombotic; blood replacement; ss.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       CCGACTTTTAATAAAATTACTCCAAATTTAGCCGAATTTGCTTTTCTTTGTATAGACAA 131
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 Expressing mature, glycosylated proteins in monocotyledonous plant cells - from chimeric gene including signal peptide sequence, specifically therapeutic agents and industrial enzymes
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          41.2%; Score 628.4; DB 19; Length 1260; 70.7%; Pred. No. 5.4e-148; Live 0; Mismatches 346; Indels 0;
                                                                                                                                                                       l..75
/*tag= a
/note= "codon-optimised RAmy3D signal sequence"
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        Sequence 1260 BP; 287 A; 428 C; 350 G; 195 T; 0 other;
                                                                                                                                                                                                                                                /*tag= b
/note= "encodes mature AAT"
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            Disclosure; Pages 34 iii-iv; 53pp; English.
                                                                                                                                                     Location/Qualifiers
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  (PHYT-) APPLIED PHYTOLOGICS INC.
                                                                                                                                                                                                                                                                                                                                                                                                                                     97US-0037991.
97US-0038168.
97US-0038169.
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Best Local Similarity
                                                                                                                  Homo sapiens
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1092 CCACCAGAAGTTAAATTTAATAAACCATTCGTTTTTCTGATGATCGAGCAGAACACTAAA 1151
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TICGCCATGITGAGITITAGGIACIAAAAGCCGAIACCCAIGACGAGAITITAGAAGGITIA
                                                                252 AACTITAATITGACCGAAATCCCAGAAGCCCAAATTCACGAGGGTTTTCAAGAGTTGTTG
                                                                                                                               AGAACTTTGAATCAACCTGATTCTCAATTGCAATTAACTACTGGTAACGGTTTATTTTG
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          192 ITCGCCATGTTGAGTTTAGGTACTAAAGCCGATACCCATGACGAGATTTTAGAAGGTTTA 251
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   72 CCGACTTTTAATAAAATTACTCCAAATTTAGCCGAATTTGCTTTTTCTTTGTATAGACAA 131
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             0; Gaps
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         The sequence of a human alpha-1-antitrypsin cDNA clone is given in AAQ89254. Expression of the cDNA in host cell transformants has allowed production of recombinant alpha-1-antitrypsin.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   220 CIGGCACACCAGCCAACAGCACCAATATCTTCTTCTCCCCAGTGAGCATCGCTACAGCC
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             Human alphal-antitrypsin (al-AT) cDNA sequence - can be used for
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             Query Match 28.3%; Score 432.2; DB 16; Length 1312; Best Local Similarity 60.4%; Pred. No. 1.1e-98; Matches 713; Conservative 0; Mismatches 468; Indels 0;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        Sequence 1312 BP; 339 A; 368 C; 324 G; 281 T; 0 other;
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                                                                                                                                                        Alpha-1-trypsin; protease-inhibitor; ss
                                                                                                                                                                                                                                       Cocation/Qualiflers
28..1258
AAQ89254 standard; cDNA; 1312 BP
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8705-0133190
8705-0133190
8905-0246912
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9105-0566450
9305-0966425
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28.99
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100.1255
/*tag= c
                                                                                                                    Human alpha-1-trypsin cDNA
                                                                             (first entry)
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                                                                                                                                                                                               Homo sapiens
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                                                                             18-OCT-1995
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18-NOV-1992;
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03-MAR-1987
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22-AUG-1989
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1032 GATGAAAAGGGTACCGAGGCCGCGCGCTATGTTCCTGGAAGCTATTCCAATGAGCAT 1091
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                               AAAGATACTGAAGAGGAAGATTTTCATGTTGATCAAGTTACTACTGTCAAAGTTCCAATG 671
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            252 AACTITAATITGACCGAAATCCCAGAAGCCCAAATTCACGAGGGTTTTCAAGAGTTGTTG 311
                                                                                                               312 AGAACTTTGAATCAACCTGATTCTCAATTGCAATTAACTACTGGTAACGGTTTATTTTTG 371
                                                                                                                                                                       400 CGTACCCTCAACCAGCCAGACAGCCAGCTCCAGCTGACCACCGGCAATGGCCTGTTCCTC 459
                                                                                                                                                                                                                                  372 TCTGAAGGTTTAAAATTGGTTGACAAATTCCTAGAAGACGTCAAGAACTATATCATAGT 431
                                                                                                                                                                                                                                                                                          460 AGCGAGGCCTGAAGCTAGTGGTAAGTTTTTGGAGGATGTTAAAAAGTTGTACCACTCA 519
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312 AGAACTTTGAATCAACCTGATTCTCAATTGCAATTAACTACTGGTAACGGTTTATTTTG

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                                   Human alpha-1-antitrypsin; ATR-1; antibody; ATR-1 deficiency; ss.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   28.3%; Score 432.2; DB 19; Length 1312; ilarity 60.4%; Pred. No. 1.1e-98; Conservative 0; Mismatches 468; Indels 0;
                                                                                                                                                                                                                                                                                                                                                                                                                                                        DNA encoding alpha-1 anti-trypsin - useful for, e.g. producing recombinant alpha-1 anti-trypsin
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           Sequence 1312 BP; 339 A; 368 C; 324 G; 281 T; 0 other;
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/product= "alpha-1-antitrypsin"
         Nucleotide sequence of the alpha-1-antitrypsin
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                                                                                    Location/Qualifiers
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87US-0022543.
87US-0133190.
88US-0246912.
89US-0398288.
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P-PSDB; AAW56709.
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                                                                                                                                                                                                                                                   03-MAR-1987;
15-DEC-1987;
16-SEP-1988;
22-AUG-1989;
11-MAR-1991;
                                                             Homo sapiens
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02-JUL-1993;
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Matches
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940 AGAAGGICIGCCAGCITACAITIACCCAAACIGICCAITACIGGAACCIAIGAICIGAAG 999
                                                                                                                                                                                                                                                                                                                      672 AIGAAAAGACIGGGIAIGIICAAIAIICAACAIIGCAAAAAAIIAAGIICIIGGGICIIA 731
                                                                                                                                                                                                                                                                                                                                                                            Alphal-antitrypsin; neutrophil elastase inhibitor; human; ss; chronic obstructive pulmonary emphysema; infantile liver cirrhosis.
                                                   580 GTGGAGAAGGGTACTCAAGGGAAATTGTGGATTTGGTCAAGGAGCTTGACAGAGACACA
                                                                                                                                                                                                                                                                              372 TCTGAAGGTTTAAAATTGGTTGACAAATTCCTAGAAGACGTCAAGAAACTATATCATAGT
                                                                                                                                                    GITGAGAAAGGCACCCAGGGTAAGATCGTTGACCTAGTTAAAGAATTAGATCGTGATACC
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                                                                                             432 GAGGCTTTTACCGTTAATTTTGGTGATACTGAGGAAGCTAAAAAGCAAATTAATGATTAT
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                                                                                                                                                                                                                                                                                                                                                                                                                          This sequence represents the human alphal-antitrypsin nucleotide sequence. Alphal-antitrypsin is an important protease inhibitor, the major function of which is to inhibit neutrophil elastase. Low levels of alphal-antitrypsin in the blood are associated with chronic obstructive pulmonary emphysema and infantile liver cirrhosis. A vector comprising a mammalian alphal-antitrypsin DNA sequence that hybridises to human alphal-antitrypsin can be introduced into a host cell in a method for the production of alphal-antitrypsin.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      CCGACTTTTAATAAAATTACTCCAAATTTAGCCGAATTTGCTTTTCTTTGTATAGACAA 131
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         CCAACCTTCAACAAGATCACCCCCAACTTGGCTGAGTTCGCCTTCAGCCTATACCGCCAG 219
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                CTGGCACACCAGTCCAACAGCACCAATATCTTCTTCTCCCCAGTGAGCATCGCTACAGCC 279
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          TTCGCCATGTTGAGTTTAGGTACTAAAGCCGATACCCATGACGAGATTTTAGAAGGTTTA 251
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            AACTTTAATTTGACCGAAATCCCAGAAGCCCAAATTCACGAGGGTTTTCAAGAGTTGTTG 311
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    AATTICAACCICACGGAGATICCGGAGGCICAGAICCAIGAAGGCIICCAGGAACICCIC 399
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             AGAACTITGAATCAACCTGATTCTCAATTGCAATTAACTACTGGTAACGGTTTATTTTTG 371
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             CGTACCCICAACCAGCCAGCCAGCTCCAGCTGACCACCGGCAATGGCCTGTTCCTC 459
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    GAAGACCCTCAAGGCGACGCCGCTCAAAAACCGGACACCAGTCATCACGACCAAGACCAT 71
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        132 TTAGCTCATCAAAGTAATTCTACTAACATTTTTTTTTAGTCCTGTTTCTATTGCCACTGCT
                                                                                                                                                                                                                                                                                                                                      Preparing alphal-antitrypsin for inhibiting neutrophil elastase involves transfecting host cell with vector comprising alphal-antitrypsin DNA sequence that hybridizes to human alphal-antitrypsin cDNA, or its complement -
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      DB 21; Length 1312;
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     Score 432.2; DB 21; Length
Pred. No. 1.1e-98;
0; Mismatches 468; Indels
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            Sequence 1312 BP; 339 A; 368 C; 324 G; 281 T; 0 other;
                                                                                                                                                                                                                                                                            Davie
                                                                                                                                                                                                                                                                          Woo SLC, Thirumalachary C, Kurachi K,
                                                                                                                                                                                                                                                                                                                                                                                                     Claim 1; Fig 1; 16pp; English.
                                                                                                                                               87US-0022543.
87US-0133190.
88US-0246912.
                                                                                                                                                                                   89US-0398288.
91US-0666450.
92US-0979556.
                                                                                                                                                                                                                                                  (WASH-) WASHINGTON RES FOUND
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     28.3%;
                                                                                                                       82US-0380810.
84US-0638980.
                                                                                    98US-0009581
                                                                                                            95US-0479545
                                                                                                                                                                                                                         93US-0086442
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              Matches 713; Conservative
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 Local Similarity
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           Homo sapiens
                                                                                    20-JAN-1998;
                                  US6025161-A.
                                                            15-FEB-2000
                                                                                                                                   07-FEB-1984
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16-SEP-1988
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11-MAR-1991
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           1120 GACGAGAAAGGGACTGAAGCTGCTGGGGCCATGTTTTAGAGGCCATACCCATGTCTATC 1179
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  1180 CGCCCCGAGGTCAAGTTCAACAAACCCTTTGTCTTTAATGATTGAACAAAATACCAAG 1239
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                1092 CCACCAGAAGTTAAAATTAAAACCATTCGTTTTTCTGATGATGAGGAGAACACTAAA 1151
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                                                  460 AGCGAGGGCCTGAAGCTAGTGGATAAGTTTTTGGAGGATGTTAAAAAGTTGTACCACTCA 519
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           ischemia reperfesion injury; haematopolesis; cancer; neuropathy; transgentc animal; Alzheimer's disease; Parkinson's disease; burn; amyotrophic lateral sclerosis; platelet disorder; thrombocytopenia; oulcer; osteoporosis; bone degenerative disorder; periodontal disease; gut protection; lung; liver fibrosis; immune deficiency; infection;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      Human; secreted protein; arthritis; Crohn's disease; sepsis; shock;
                                                                                                                                                                                                                                                                                                                                                                                                                                      852 CGTCGTAGCGCTTCTCTGCACCTGCCAAAGTTAAGTATCACCGGTACTTACGACTTAAAA
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      1000 AGCGTCCTAGGTCAACTGGGCATCACTAAGGTCTTCAGCAATGGGGGTGACCTCTCCGGG
372 TCTGAAGGTTAAAATTGGTTGACAAATTCCTAGAAGACGTCAAGAACTATATCATAGT
                                                                                                  432 GAGGCTTTTACCGTTAATTTTGGTGATACTGAGGAAGCTAAAAAGCAAATTAATGATTAT
                                                                                                                                                                                                    492 GTTGAGAAAGGCACCCAGGGTAAGATCGTTGACCTAGTTAAAGAATTAGATCGTGATACC
                                                                                                                                                                                                                                 640 GITITIGCICIGGIGAATIACAICTICITIAAAGGCAAAIGGGAGAGACCCITIGAAGIC
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           672 ATGAAAAGACTGGGTATGTTCAATATTCAACATTGCAAAAATTAAGTTCTTGGGTCTTA
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             792 CAACATTTAGAGAATGAGTTGACTCATGACATTATTACTAAATTTTTAGAGAACGAGGAT
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       940 AGAAGGTCTGCCAGCTTACATTTACCCAAAACTGTCCATTACTGGAACCTATGATCTGAAG
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       972 GTTACTGAAGAAGCTCCATTAAAATTGAGTAAAGCTGTTCACAAAGCCGTCTTAACTATT
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              GATGAAAAGGCTACCGAGGCCGCCGCCCTATGTTCCTGGAAGCTATTCCAATGAGCATT
                                                                                                                                                    520 GAAGCCTTCACTGTCAACTTCGGGGACACCGAAGAGGCCAAGAAACAGATCAACGATTAC
                                                                                                                                                                                                                                                                                                         GTCTTCGCACTAGTTAACTATATTTTTCAAGGGTAAGTGGGAACGTCCTTTCGAGGTT
                                                                                                                                                                                                                                                                                                                                                                                                         612 AAAGATACTGAAGAGGAAGATTTTCATGTTGATCAAGTTACTACTGTCAAAGTTCCAATG
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     1152 AGCCCATTGTTATGGGTAAGGTTGTCAACCCCAACTCAGAA 1192
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AAS45052
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severe combined immunodeficiency; SCID; autoimmune disorder; allergy;
multiple sclerosis; rheumatoid arthritis; diabetes mellitus; asthma;
fertility; analgesic; pain; antigen; ss.
Homo sapiens.
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Homo sapiens.

WO200166689-A2.

13-SEP-2001.

05-MAR-2001; 2001WO-US04942

07-MAR-2000; 2000US-0519705. 19-MAY-2000; 2000US-0574454. 17-JUN-2000; 2000US-0566193. 14-JUL-2000; 2000US-0616647. 19-SEP-2000; 2000US-0665363.

(HYSE-) HYSEQ INC.

20-OCT-2000; 2000US-0693267

Tang YT, Liu C, Asundi V, Xu C, Wehrman T, Ren F, Ma Y, Zhou P; Zhao QA, Yang Y, Drmanac RT, Zhang J, Chen R, Xue AJ, Wang J;

WPI; 2001-589934/66. P-PSDB; AAU28152. Novel polypeptides and nucleic acids obtained from cDNA libraries prepared from various human tissues, for diagnosis and treatment of cancer, neurological, inflammatory, and autoimmune disorders -

Claim 1; SEQ ID No 133; 107pp; English.

The invention relates to novel isolated human secreted polypeptides (I) and (II) are useful for treating and polymolectides (II). (I) and (II) are useful for treating transgenic such as arthritis, nephritis, Crohn's disease, inclammatory conditions such as arthritis, nephritis, Crohn's disease, incolved in increasing haematopolesis, stem cell survival, bone growth are modeling. (I), (II) and modulators of (II) are useful for prophylaxis or treatment of one or more cancers. (II) is also useful for creating transgenic animals useful for studying the nivo activities of the polypeptide as well as for studying modulators of the polypeptides. (I) induces the proliferation of neural cells and regeneration of nerve and brain tissue and is useful for the treatment of central and brain tissue and is useful for the treatment of central and peripheral nervous system disease, and amyotrophic lateral sclenosis. In addition, of haematopolesis and is useful for treating myeloid activity, regulation of haematopolesis and is useful for treating myeloid activity, regulation of haematopolesis and is useful for reactivity. Tegulation of haematopolesis such as thrombocytopenia and for regeneration of bone, cartilage, tendon, ligament and/or nerve tissue growth, and in tissue repair, healing of burns, incisions, ulcers, for treating osteoporosis, osteoarthritis, bone degenerative disorders, or periodontal disease. Purthermore, (I) is also useful for reperfusion injury in various tissues, various immune deficiencies and disorders including severe combined immunodeficiency (SCID), bacterial or reperfusion injury in various tissues, various immune deficiencies and change infections, autoimmune disorders e.g. multiple sclerosis, creating the protein or regeneration and treatment of lung or liver fibrosis, rections and conditions, such as asthma or other respiratory problems. Consections and conditions, such as asthma or other respiratory problems condition, and onlity protein, carbohydrate, vitamins, minerals, induced protein or an antig

Sequence 1367 BP; 357 A; 392 C; 323 G; 295 T; 0 other;

Query Match 28.1%; Score 429.2; DB 22; Length 1367; Best Local Similarity 60.7%; Pred. No. 6.6e-98; Matches 718; Conservative 0; Mismatches 463; Indels 1; Gaps 1;

1091 TCCACCAGAAGTTAAATTTAATAAACCATTCGTTTTTCTGATGATCGAGCAGAACACTAA 1150 1031 TGATGAAAAGGGTACCGAGGCCGCCGGCGTATGTTCCTGGAAGCTATTCCAATGAGCAT 1090 945 CAGAAGGICIGCCAGCITACATITACCCAAACIGICCATTACIGGAACCIAIGAICIGAA 1004 1065 GGTCACAGGAGGCACCCCTGAAGCTCTCCAAGGCCGTGCATAAGGCTGTGCTGACCAT 1124 610 730 790 GAGGCTTTTACCGTTAATTTTGGTGAT-ACTGAGGAAGCTAAAAAAGCAAATTAATGATTA 490 704 764 824 251 AACTITAATTTGACCGAAATCCCAGAAGCCCAAATTCACGAGGGTTTTCAAGAGTTGTTG 311 312 AGAACTITGAATCAACCTGATTCTCAATTGCAATTAACTACTGGTAACGGTTTATTTTG 371 464 372 TCTGAAGGTTTAAAATTGGTTGACAAATTCCTAGAAGACGTCAAGAAACTATATCATAGT 431 524 105 GAGGATCCCCAGGGAGATGCTGCCCAGAAGACAGATACATCCCCACCATGATCAGGATCAC 164 225 CIGGCACACCAGTCCAACAGCACCAATATCTTCTTCTCCCCAGTGAGCATCGCTACAGCC 284 285 ITIGCAAIGCICICCCTGGGGACCAAGGCIGACACTCACGAIGAAAICCIGGAGGGCCIG 344 12 GAAGACCCTCAAGGCGACGCCGCTCAAAAACCGACACCAGTCATCACGACCAAGACCAT 71 AGCGAGGGCCTGAAGCTAGTGTTTTTGGAGGATGTTAAAAAGTTGTACCACTCA 585 CGTGGAGAAGGGTACTCAAGGGAAAATTGTGGATTTGGTCAAGGAGCTTGACAGAGACAC 611 TAAAGATACTGAAGAGGAAGATTTTCATGTTGATCAAGTTACTACTGTCAAAGTTCCAAT 705 CAAGGACACCGAGGACGAGGACTTCCACGTGGACCAGGTGACCACGTGAAGGTCCCTAT 671 GATGAAAAGACTGGGTATGTTCAATATTCAACATTGCAAAAAATTAAGTTCTTGGGTCTT 885 ACAGCACCTGGAAAATGAACTCACCCACGATATCATCACCCAAGTTCCTGGAAAATGAAGA 851 TCGTCGTAGCGCTTCTCTGCACCTGCCAAAGTTAAGTATCACCGGTACTTACGACTTAAA 971 IGITACTGAAGAAGCTCCATTAAAATTGAGTAAAGCTGTTCACAAAGCCGTCTTAACTAT 1125 CGACGAGAAGGGGACTGAAGCTGCTGGGGCCATGTTTTAGAGGCCATACCAATGTCTAT 491 TGTTGAGAAAGGCACCCCAGGGTAAGATCGTTGACCTAGTTAAAGAATTAGATCGTGATAC CGTCTTCGCACTAGTTAACTATTTTTTCAAGGGTAAGTGGGAACGTCCTTTCGAGGT 645 AGTITITGCTCTGGTGAATTACATCTTCTTTAAAGGCAAATGGGAGAGACCTTTTGAAGT 791 TCAACATTTAGAGAATGAGTTGACTCATGACATTATTACTAAATTTTTAGAGAACGAGGA 132 TTAGCTCATCAAAGTAATTCTACTAACATTTTTTTTTAGTCCTGTTTCTATTGCCACTGCT TICGCCATGITGAGITIAGGIACTAAAGCCGATACCCAIGACGAGAITITAGAAGGITIA 405 CGTACCCTCAACCAGCCAGACAGCTCCAGCTGACCACCGGCAATGGCCTGTTCCTC 192 252 432 525 551 Dp δλ Op g g qq Dp 원 g g ŏ g δλ g δ d g δ ŏ g ď à g ò õ g δ δ ò ŏ δ ŏ ò

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invention. The specification describes a method for producing mature invention. The specification describes a method for producing mature intention. The specification describes a method for producing mature intention or producing mature comprises transforming the cells with a chimeric gene comprising a monocotyledon transcription regulator, inducible either during seed maturation or by adding/removing a small molecule, DNA encoding the heterologous protein, and DNA encoding a small molecule, DNA encoding the heterologous protein, and DNA encoding the protein from the cell. The signal peptide causing secretion of the protein from the cell. Proteins expressed in this manner include mature giyocosylated alpha 1-antitrypsin (ANT) with a giyocosylation pattern that significantly increases its serum half-life, mature giyocosylated antithrombin III (ATII), mature human serum albumin (HSA) having the native folding pattern as shown by bilitubin-binding characteristics, or mature active subtilisin BNN'. These proteins are useful therapeutically (e.g. AAT for treating emphyseme, "Plant"), "These proteins are useful therapeutically (e.g. AAT for treating emphyseme, "The state of the protein as antithrombotic and HSA as blood replacement)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          Protein expression; monocotyledon plant cell; glycosylated antithrombin III; glycosylated alpha 1-antitrypsin; AAT; glycosylated antithrombin III; AATI; human serum albumin; HSA; subtilisin BPN'; treatment; emphysema; antithrombotic; blood replacement; ss.
present sequence represents the native coding sequence of mature
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       plant
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           Native coding sequence of mature alphal-antitrypsin (AAT)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                Sequence 1185 BP; 328 A; 324 C; 283 G; 250 T; 0 other;
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                                                                                                                                                                     1245 GTCTCCCCTCTTCATGGGAAAAGTGGTGAATCCCACCCAAAA 1286
                                                                                                                         1151 AAGCCCATTGTTATGGTAAGGTTGTCAACCCCAACTCAGAA 1192
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            (PHYT-) APPLIED PHYTOLOGICS INC
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97US-0037991.
97US-0038168.
97US-0038169.
                                                                                                                                                                                                                                                                                                                                                                                                                    AAV41726 standard; DNA; 1185
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         (first entry)
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P-PSDB; AAW59839.
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  13-FEB-1998;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          L3-FEB-1997;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         20-NOV-1998
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  AAV41726;
                                                                                                                                                                                                                                                                                                                                     RESULT 13
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GATGAAAAGGGTACCGAGGCCGCCGCGCTATGTTCCTGGAAGCTATTCCAATGAGCATT 1091
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  1021 GACGAGAAAGGGACTGAAGCTGCTGGGGCCATGTTTTAGAGGCCATACCCATGTCTATC 1080
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           GTTACTGAAGAAGCTCCATTAAAATTGAGTAAAGCTGTTCACAAAGCCGTCTTAACTATT 1031
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                                                                                                                                                                                                                                                                                                                                                     431
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               672 ATGAAAAGACTGGGTATGTTCAATATTCAACATTGCAAAAAATTAAGTTCTTGGGTCTTA 731
                                                                       61 CCAACCTICAACAAGATCACCCCCAACCTGGCTGGGTTCGGCTTTCAGCCTATACCGCCAG 120
                                                                                                                                                                          251
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                                                                                                                   TTAGCTCATCAAAGTAATTCTACTAACATTTTTTTTTAGTCCTGTTTCTATTGCCACTGCT
                                                                                                                                                                                                                                                                                                                                                     372 TCTGAAGGTTTAAAATTGGTTGACAAATTCCTAGAAGACGTCAAGAAACTATATCATAGT
                                                                                                                                                                                                                                                                                                                                                                                                                                                                       GTTGAGAAAGGCACCCAGGGTAAGATCGTTGACCTAGTTAAAGAATTAGATCGTGATACC
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                  TTCGCCATGTTGAGTTTAGGTACTAAAGCCGATACCCATGACGAGATTTTAGAAGGTTTA
                                                                                                                                                                                                      181 TITGCAATGCTCTCCCTGGGACCAAGGCTGACACTCACGATGAAATCCTGGAGGGCCTG
                                                                                                                                                                                                                                   AACTTTAATTTGACCGAAATCCCAGAAGCCCCAAATTCACGAGGGTTTTCAAGAGTTGTTG
                                                                                                                                                                                                                                                  312 AGAACTTTGAATCAACCTGATTCTCAATTGCAATTAACTACTGGTAACGGTTTATTTTG
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28.1%; Score 429; DB 19; Length 1185; 60.2%; Pred. No. 7.1e-98; 1.1ve 0; Mismatches 470; Indels 0

Best Local Similarity 60.2 Matches 711; Conservative

**Ouery Match** 

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192
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           A plasmid consisting of a pCMV4 expression vector including a coding sequence of human alpha-1 antitrypsin may be incorporated into liposomes capable of targeting specific tissue. The plasmid is then capable of expression of the gene extrachromosomally in the cells of the target tissue. Thus, the liposome including the cells of the target tissue. Thus, the liposome including the plasmid can be used in a method for treating a deficiency of the plasmid can be used in a method for treating a deficiency of the capacitic use of the human alpha-1 antitrypsin is significant as this antiprotease is important in protecting the lungs against to involve a relative deficiency of antiprotease activity.

C Therefore, the delivery of a functioning alpha-1 antiprotease of the functioning alpha-1 antiprotease capacitic in many human conditions
1081 CCCCCCGAGGTCAACAACAAAAACCCTTTGTCTTAATGATTGAACAAAATACCAAG 1140
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          152 CCAACCTTCAACAAGATCACCCCCAACCTGGCTGAGTTCGCCTTCAGCCTATACCGCCAG 211
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       132 TTAGCTCATCAAAGTAATTCTACTAACATTTTTTTTAGTCCTGTTTCTATTGCCACTGCT 191
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  92 GAGGATCCCCAGGGAGATGCTGCCCAGAAGACAGATACATCCCCACCATGATCAGGATCAC 151
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               12 GAAGACCCTCAAGGCGACGCCGCTCAAAAAACCGACACCAGTCATCATCACGACCAAGACCAT 71
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            ;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        Human alpha-1 anti-trypsin contg. plasmid - for treatment of anti-protease deficiency in emphysema and other lung diseases
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               Length 1352;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            Score 429; DB 13; Length 1:
Pred. No. 7.4e-98;
0; Mismatches 470; Indels
                                                                                                                                                                                                                                                                 emphysema;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 Sequence 1352 BP; 349 A; 386 C; 325 G; 292 T; 0 other;
                                           1152 AGCCCATTGTTATGGGTAAGGTTGTCAACCCAACTCAGAA 1192
                                                                     1141 rerecererreareseananeresereneereereenen 1181
                                                                                                                                                                                                                                                            Plasmid; pCMV4; liposome; antiprotease; lung; adult respiratory distress syndrome; ARDS; ss.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  Canonico A, Conary J, Meyrick B;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  Disclosure; Fig 6a-6b; 32pp; English.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       characterised by injury of the lungs.
                                                                                                                                              AAQ31403 standard; DNA; 1352
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60.2%;
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                                                                                                                                                                                                       (first entry)
                                                                                                                                                                                                                                 Human alpha-1 antitrypsin.
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                                                                                                                                                                                                                                                                                                                                                                                                                        24-APR-1991;
                                                                                                                                                                                                                                                                                                                                                                                          27-MAR-1992;
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                                                                                                                                                                         AAQ31403;
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212 CTGGCACACCAGTCCAACAGCACCAATATCTTCTCCCCCAGTGAGCATCGCTACAGCC 271
                                                                                        TICGCCATGITGAGITIAGGIACIAAAGCCGAIACCCAIGACGAGAITITAGAAGGITIA 251
                                                                                                                                                                                                                 252 AACTTTAATTTGACCGAAATCCCAGAAGCCCAAATTCACGAGGGTTTTCAAGAGTTGTTG 311
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                                                                                                                               452 AGCGAGGGCCTGAAGCTAGTGGATAAGTTTTTGGAGGATGTTAAAAAGTTGTACCACTCA
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          312 AGAACTTTGAATCAACCTGATTCTCAATTGCAATTAACTACTGGTAACGGTTTATTTTG
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Human; cancer; colon; breast; ovary; oesophagus; kidney; thyrold;
stomach; lung; prostate; pancreas; carcinoma; antitumour; cancerous;
cytostatic; gene therapy; antineoplastic; Wilm's tumour; adenocarcinoma;
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         Endress G,
                                                                                                                                                                                                                                                   Thyroid cancer related gene sequence SEQ ID NO:5848.
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                                       ABL67511 standard; DNA; 1352 BP
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2000US-235082P
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2000US-23537P
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Weaver Z;
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The present invention describes a method (M1) for screening for an anti-neoplastic agent. The method involves exposing cells to a chemical agent to be tested for anti-neoplastic activity, determining a change in expression of at least one gene (I) of a signature gene set, where (I) comprises a sequence (S) selected from 8447 sequences (given in ABL61664 to ABL70110), or is at least 95% identical to (S), where a change in expression is indicative of anti-neoplastic activity. (I) has cytostatic activity and can be used in gene therapy. MI can be used for screening an anti-neoplastic agent, and can be used for producing a product which is the data collected with respect to the anti-neoplastic agent as a result of M1, and the data is sufficient to convey the chemical structure and/or properties of the agent. MI can be used in the treatment of cancer such as colon, breast, stomach, lung, thyroid, cesophageal, ovarian, kidney, prostate or pancrealic cancer, adenocarcinoma, carcinoma, clear cell cancer, infiltrating ductal cancer, infiltrating lobular cancer, squamous cell cancer infiltrating ductal cancer, infiltrating lobular cancer.
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              332 AATITCAACCICACGGAGATICCGGAGGCICAGAICCAIGAAGGCIICCAGGAACICCIC 391
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chemical agent to be tested for anti-neoplastic activity, and determining a change in expression of a gene of a signature gene set
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                                                                                                                                                                                                                                                                                                                                                                                                                                  carcinoma, papillary carcinoma and Wilm's tumour.
                                                             Claim 1; SEQ ID 5848; 44pp; English.
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